

REMARKS:

Claim 1 has been amended so as to include the limitations of claims 3 and 4, as discussed below.

Support for new claim 9 may be found at least at page 6, lines 1-15.

Claim 1 has been amended as requested by the examiner.

The abstract has been re-written.

Regarding the sequence listing issues, applicant notes that a paper nucleotide sequence listing was submitted on October 17, 2005 as noted by the USPTO in the Notification of Missing Requirements mailed August 11, 2006.

Regarding Figure 5, applicant respectfully notes that the sequence identification numbers may be found in the description of Figure 5. However, a replacement Figure 5 with the sequence identifiers listed thereon is enclosed herewith for the convenience of the examiner.

Regarding page 18, applicant respectfully notes that all of the sequences listed on that table include a sequence identifier and may be found in the sequence listing originally filed.

Regarding page 11, it is noted that two of the sequences listed do not appear in the sequence listing originally submitted. These sequences have been designated as SEQ ID No. 26 and SEQ ID No. 27 and replacement electronic and paper copies of the sequence listing are enclosed herewith.

Claims 1-2 were rejected under 35 USC 102(b) as anticipated by Loparev et al (J Clin Microbiol 39: 94-100). It is believed that the amendment of claim 1 to include the limitations of claims 3 and 4 overcomes this objection.

Claims 3-4 were rejected under 35 USC 103(a) as unpatentable over Loparev in view of Lowe et al (NAR 18: 1757-1761).

Specifically, the office action states that while 'Loparev et al did not specifically teach a primer pair comprising 12 or more consecutive nucleotides of SEQ ID No. 1 and 2 or SEQ ID No. 3 and 4... Lowe et al teach a method for designing primers from known sequences and evaluating their performance...'

The office action further states that 'selection of specific oligonucleotides for specific T<sub>m</sub> represents routine optimization with regard to sequence, length and composition of the oligonucleotide, which routine optimization parameters are explicitly recognized in Lowe et al.'

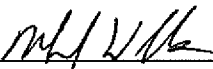
It is respectfully requested that the examiner reconsider this objection. Specifically, the selection of the primers in the instant invention was not a matter of the optimization of conditions. Furthermore, the selection of primers was not done using any algorithm. The first step necessary was locating regions of the target gene that are sufficiently conserved for the placement of primers that would ensure that all orthopoxviruses of concern would be amplified, that is, is highly conserved across different orthopoxviruses. This region must be of a size suitable for rapid and efficient amplification but large enough to naturally contain the restriction enzyme sites that are used to distinguish different viruses. It is important to note that the restriction enzyme sites were not added by the inventors but occur naturally and are conserved in all

known examples of that particular virus. As the examiner will appreciate, this makes the selection of primer pairs very difficult as they must amplify a suitably sized region of target DNA from well conserved primer sites and this region must contain unerringly present restriction enzyme sites for the RFLP analysis. A computer program simply determining which primer sets are useful for amplification would not be able to select the primer sets used.

Accordingly, applying the computer program described by Lowe wherein the computer program selects primers which enhance primer-to-target sequence hybridization avidity at 3'-end extension initiation sites, facilitate attainment of full length extension during the 72°C phase and limit primer losses due to primer-self or primer-primer homologies to the orthopoxvirus sequences described in Loparev would produce primers with the optimum characteristics for amplification, that is, the best primers for amplifying regions of the *crmB* gene. However, the primer sets described by applicants are not simply optimized primers for amplification but rather are primers which hybridize to specific highly conserved regions of the orthopoxvirus genome AND are positioned such that the resulting amplicon will include one or more specific restriction enzyme sites which can be used to identify the orthopoxvirus in the sample. As noted above, primer sets having these useful features cannot simply be identified using a computer algorithm.

Further and more favorable consideration is respectfully requested.

Respectfully submitted  
Markus Czub et al.

PER:   
Michael R. Williams  
Registration 45,333

Winnipeg, Manitoba, Canada  
Telephone (204) 944-0034 FAX (204) 942-5723